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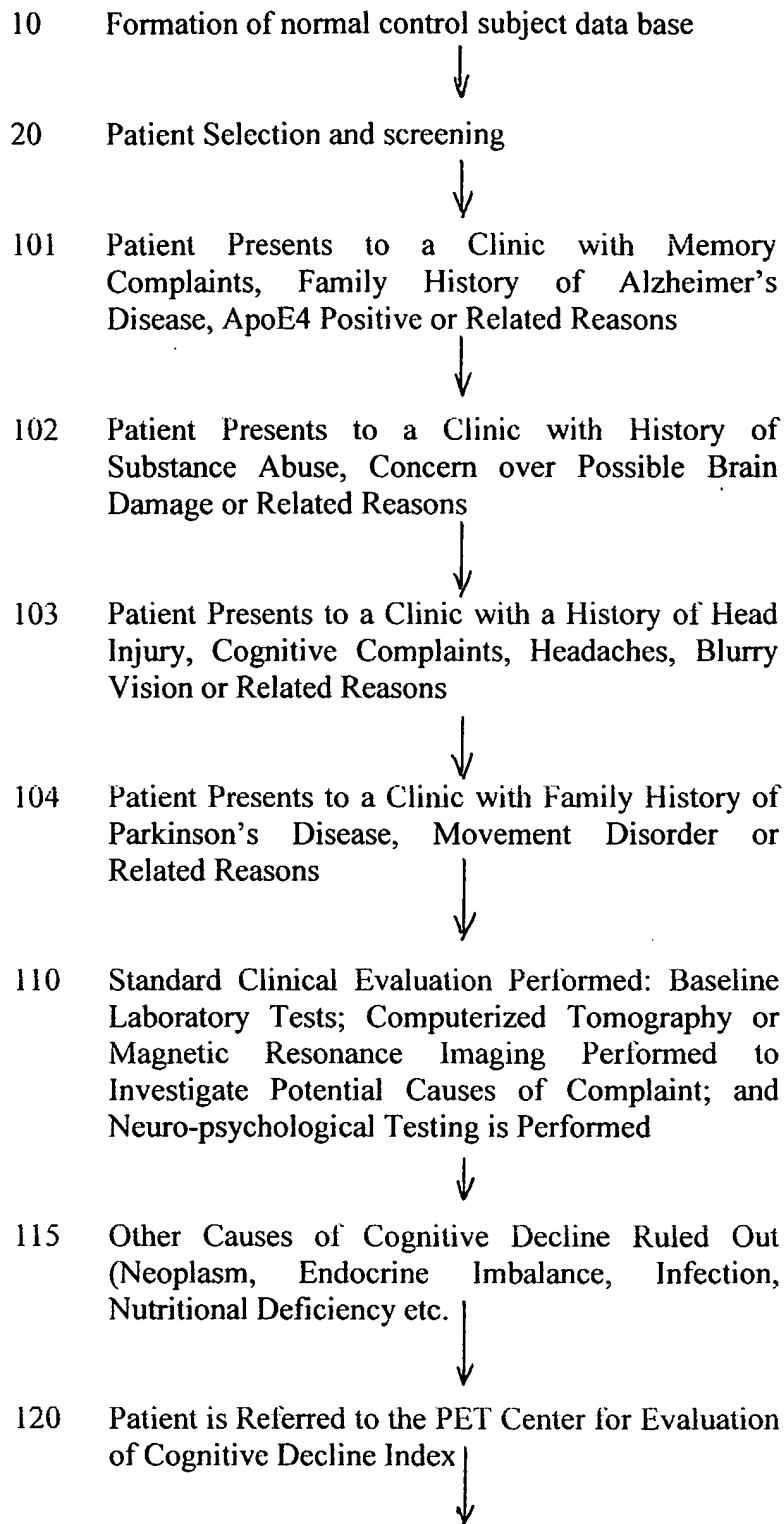
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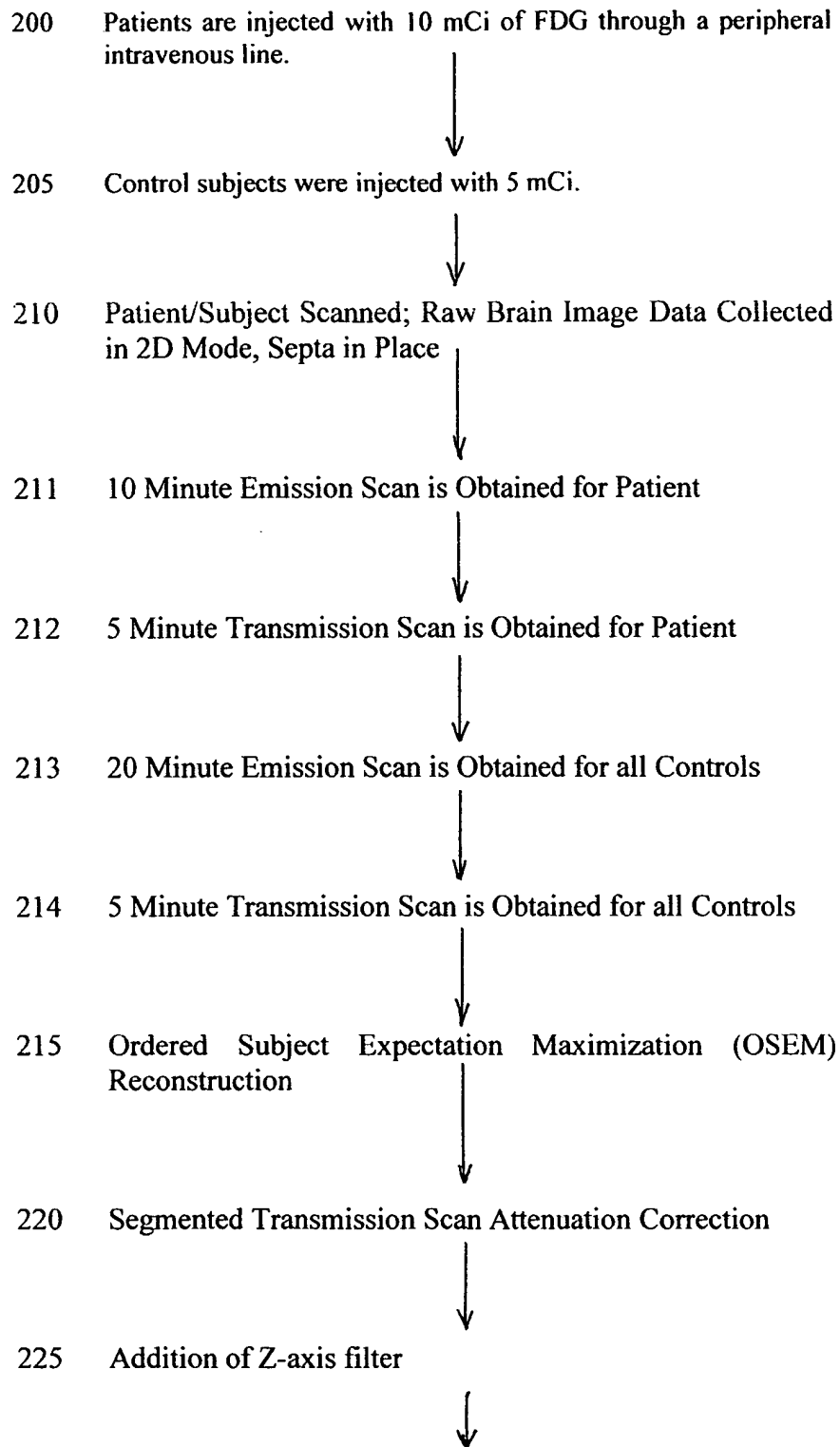
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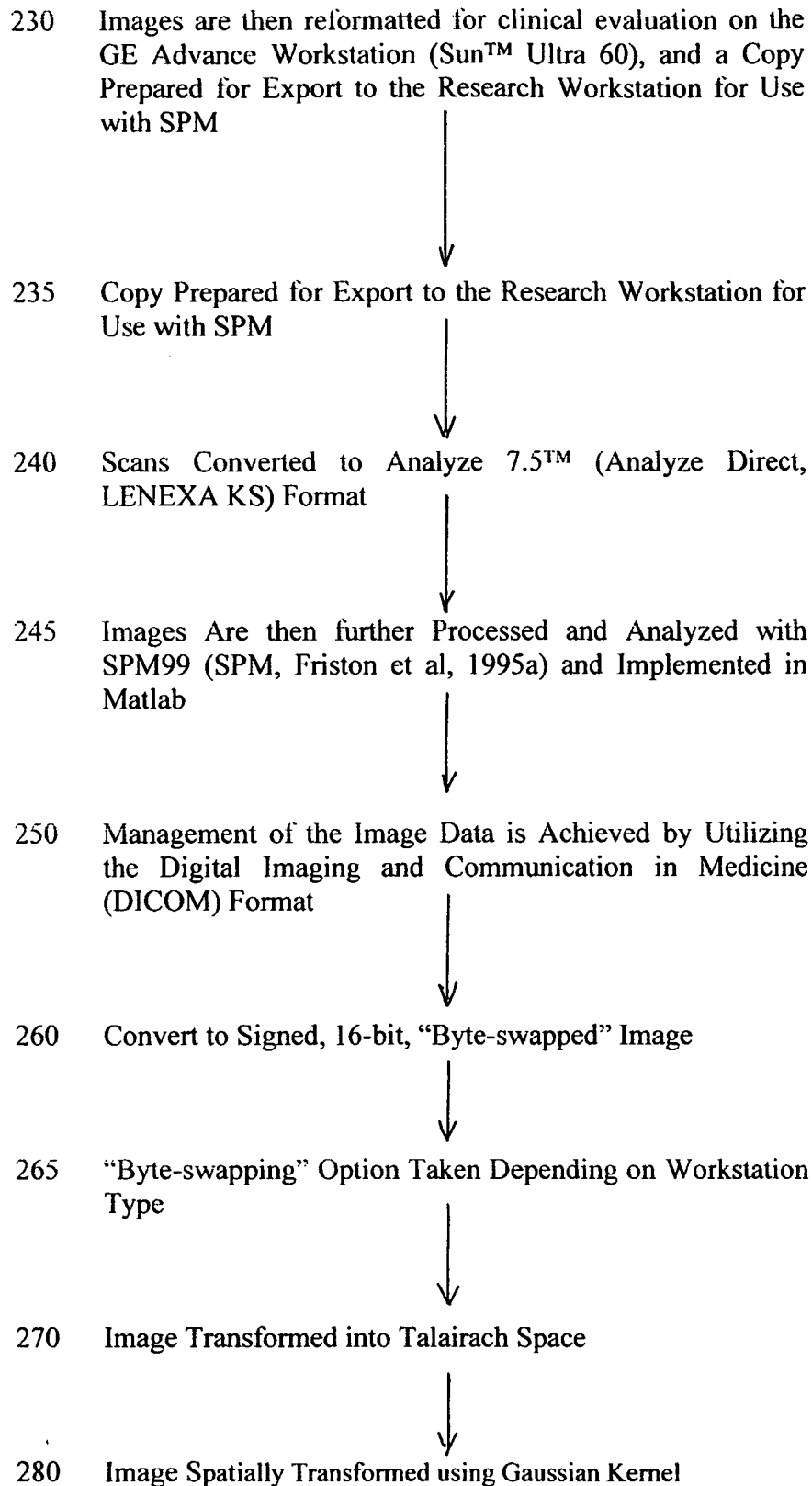
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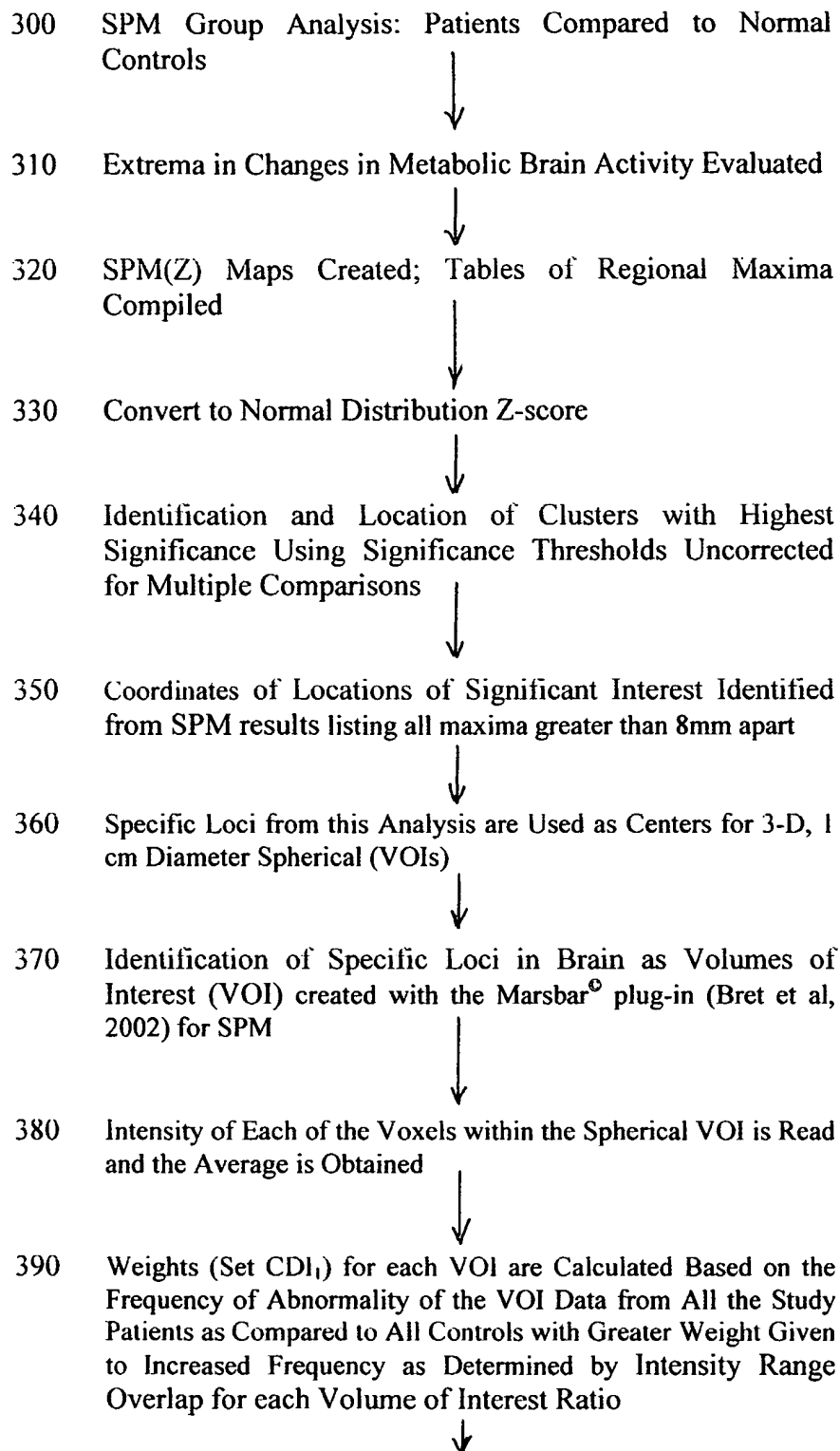
**FIG. 1 Normal Subject Controls and Patient Selection for Development of the Cognitive Decline Index**



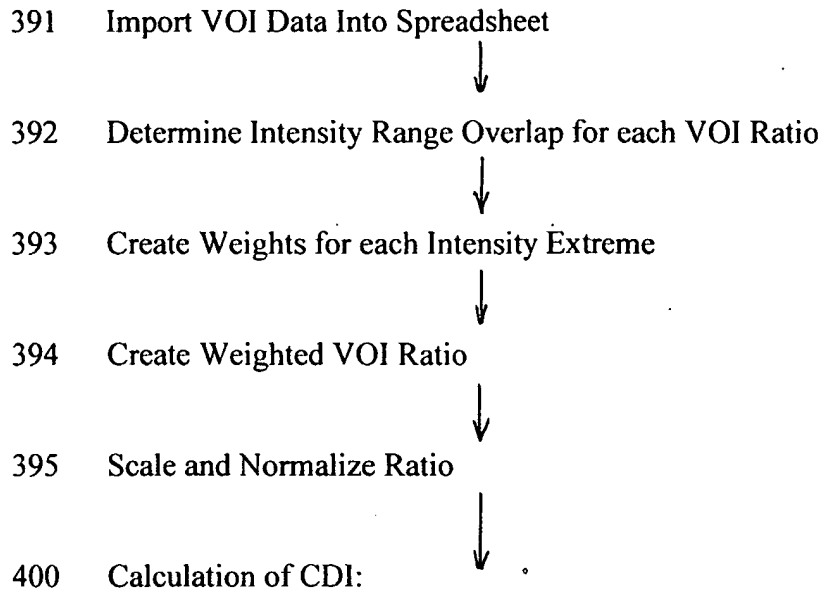
**FIG. 2a Derivation of the Processed Digital Brain Image**



**FIG. 2a (Cont'd) Derivation of the Processed Digital Brain Image**



**FIG. 2b Derivation of Region Location and Identification of VOIs**



$$CDI = C_x + \left[ \sum_{j=1}^n V_j X_j / n \right] / \left[ \sum_{i=1}^m W_i Y_i / m \right]$$

Where  $X_j$  denotes the  $j^{\text{th}}$  Increased Intensity Value;

$V_j$  denotes the  $j^{\text{th}}$  Weight for the  $j^{\text{th}}$  Increased Intensity Value;

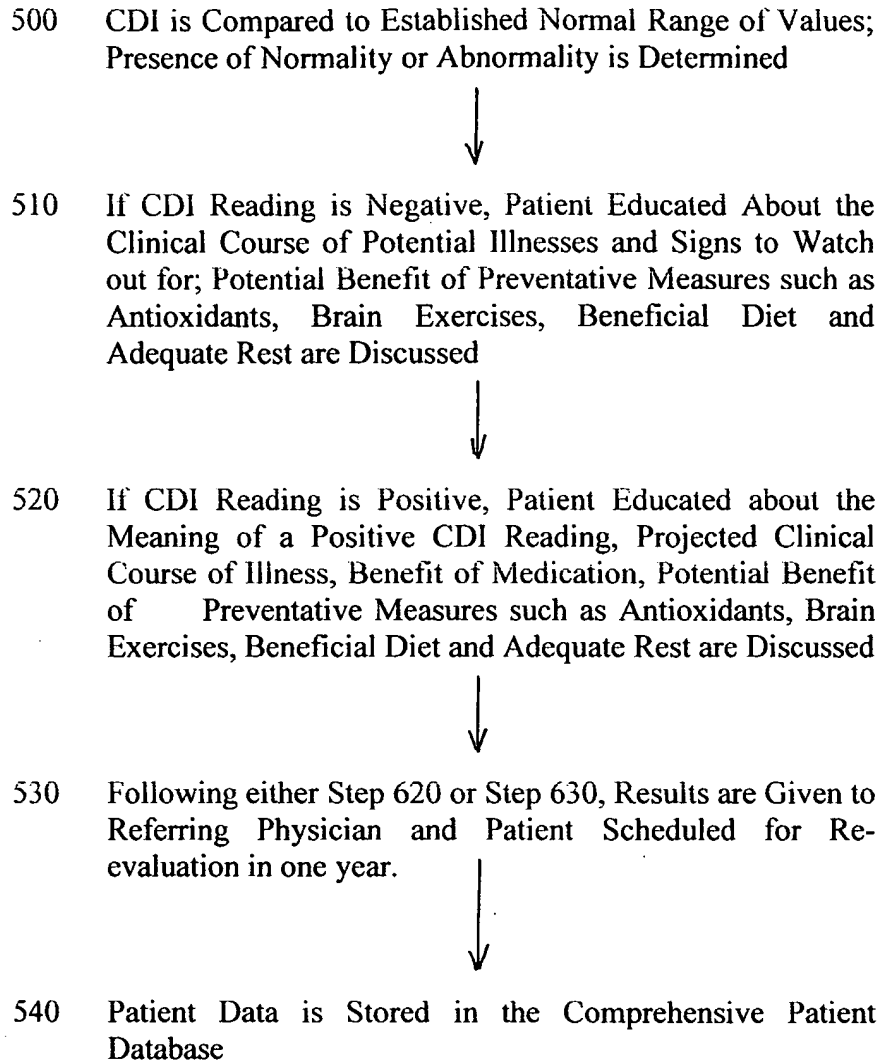
$Y_i$  denotes the  $i^{\text{th}}$  Decreased Intensity Value; and

$W_i$  denotes the  $i^{\text{th}}$  Weight for the  $i^{\text{th}}$  Decreased Intensity Value.

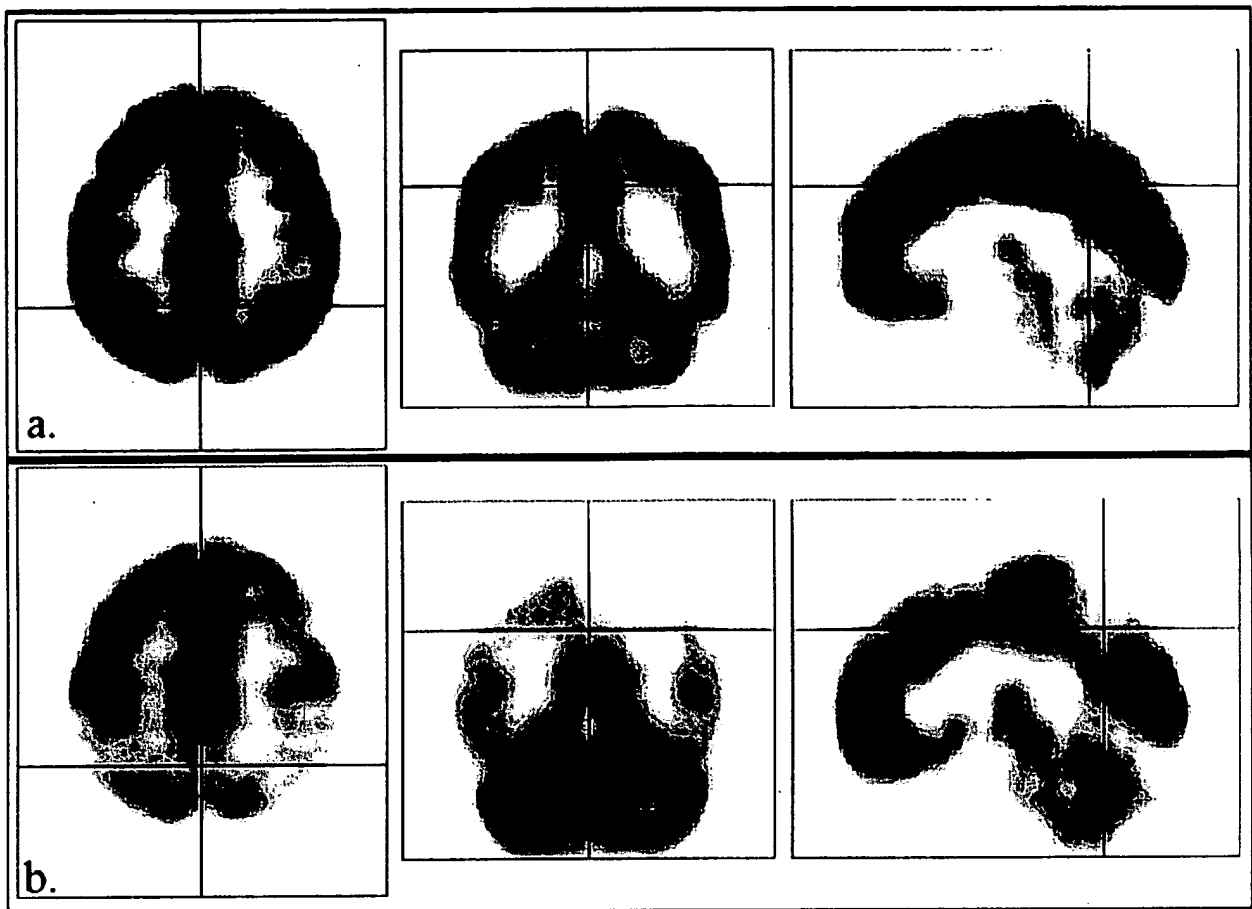
$C_x$  is the correction factor used to normalize the dataset.

- 410 Weights of Set  $CDI_1$  are then used as a baseline for calculation of a second set of Weights (Set  $CDI_2$ ) to calculate  $CDI_2$ . Set  $CDI_2$  is calculated by iterative optimization of each weight to maximally separate the patient from the controls

**FIG. 2b (Cont'd) Derivation of Region Location and Identification of VOIs**



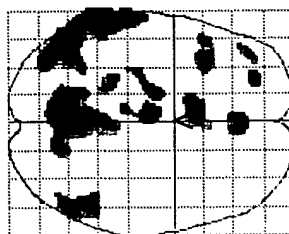
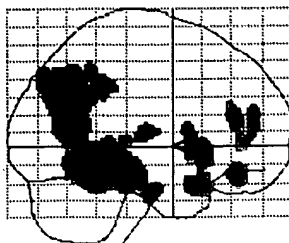
**FIG. 2c Patient Diagnosis and Clinical Recommendations**



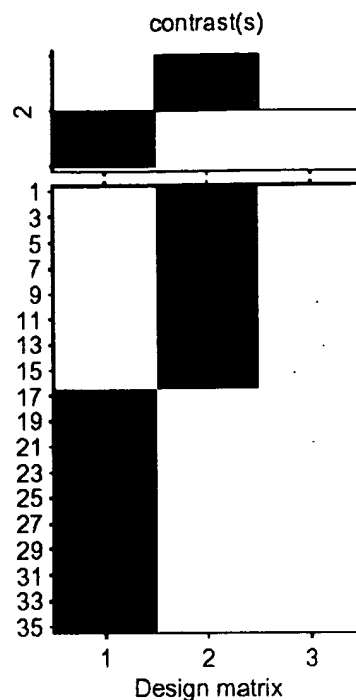
**Fig. 3**



SPMnip  
[0, 0, 0]



SPM{T<sub>33</sub>}



**SPMresults:** results, 122802 MCivsGldctrls  
Height threshold T = 2.50  
Extent threshold k = 50 voxels

**Statistics: volume summary (p-values corrected for entire volume)**

set-level		cluster-level			voxel-level				x,y,z (mm)
p	c	p <sub>corrected</sub>	k <sub>F</sub>	p <sub>uncorrected</sub>	p <sub>corrected</sub>	T	(Z)	p <sub>uncorrected</sub>	
0.173	14	0.000	1945	0.000	0.106	5.29	(4.47)	0.000	-4 -70 30
					0.483	4.54	(3.97)	0.000	-14 -68 16
					0.616	4.37	(3.86)	0.000	-4 -58 28
		0.000	2610	0.000	0.788	4.16	(3.70)	0.000	-42 -74 36
					0.804	4.13	(3.68)	0.000	-56 -56 16
					0.881	4.01	(3.59)	0.000	-60 -56 -8
		0.862	202	0.064	0.883	4.01	(3.59)	0.000	-6 14 -24
		0.247	450	0.009	0.951	3.84	(3.47)	0.000	52 -64 38
					1.000	2.96	(2.77)	0.003	54 -50 44
		1.000	58	0.302	0.998	3.49	(3.20)	0.001	-48 18 -22
		0.991	114	0.153	0.998	3.48	(3.19)	0.001	-4 -12 10
					1.000	2.81	(2.64)	0.004	-8 -30 4
		0.996	101	0.177	0.999	3.43	(3.15)	0.001	4 38 -16
		0.944	162	0.093	1.000	3.37	(3.10)	0.001	-10 14 -2
					1.000	2.90	(2.71)	0.003	-12 8 12
		0.981	131	0.127	1.000	3.32	(3.07)	0.001	-20 -14 -28
					1.000	2.91	(2.72)	0.003	-30 -22 -20
		0.888	191	0.071	1.000	3.22	(2.98)	0.001	-38 20 -2
		0.997	95	0.189	1.000	3.21	(2.97)	0.001	-26 48 16
		0.993	110	0.160	1.000	3.05	(2.84)	0.002	-2 36 18
					1.000	2.69	(2.54)	0.006	-2 42 2
		1.000	69	0.261	1.000	3.00	(2.80)	0.003	-24 -38 -6
		1.000	50	0.338	1.000	2.93	(2.74)	0.003	-40 46 6

table shows at most local maxima > 8.0mm apart per cluster

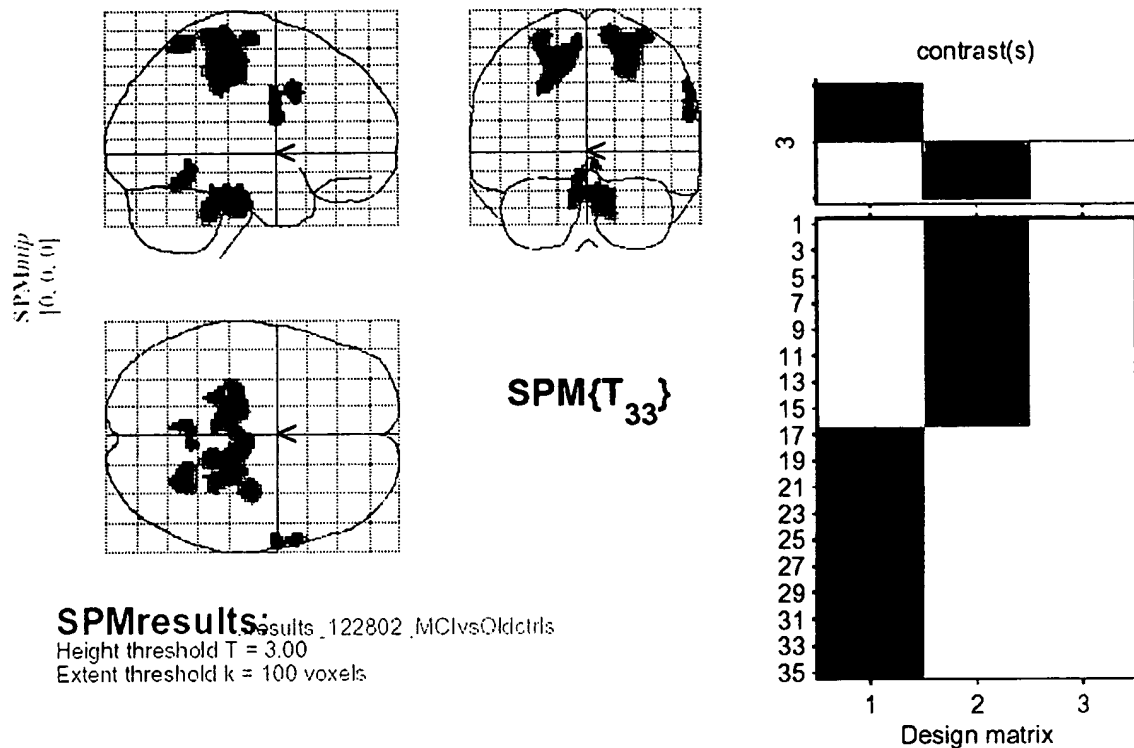
Height threshold: T = 2.50, p = 0.009 (1.000 corrected)  
Extent threshold: k = 50 voxels, p = 0.338 (1.000 corrected)  
Expected voxels per cluster, <k> = 58.849  
Expected number of clusters, <c> = 10.48  
Degrees of freedom = [1.0, 33.0]  
Smoothness FWHM = 13.5 13.7 16.0 (mm) = 6.7 6.9 8.0 (voxels)  
Search volume: S = 1815544 mm<sup>3</sup> = 226943 voxels = 559.8 resels  
Voxel size: [2.0, 2.0, 2.0] mm (1 resel = 370.95 voxels)

**Statistics: single cluster summary (p-values corrected for entire volume)**

cluster-level			voxel-level				x,y,z (mm)
p <sub>corrected</sub>	k <sub>F</sub>	p <sub>uncorrected</sub>	p <sub>corrected</sub>	T	(Z)	p <sub>uncorrected</sub>	
0.000	2610	0.000	0.788	4.16	(3.70)	0.000	-42 -74 36
			0.804	4.13	(3.68)	0.000	-56 -56 16
			0.881	4.01	(3.59)	0.000	-60 -56 -8
			0.892	3.99	(3.58)	0.000	-62 -36 -6
			0.905	3.96	(3.56)	0.000	-64 -30 -22
			0.938	3.89	(3.50)	0.000	-58 -46 -22
			0.977	3.74	(3.39)	0.000	-50 -60 42
			0.987	3.66	(3.33)	0.000	-42 -62 44
			0.998	3.50	(3.21)	0.001	-52 -62 28
			1.000	3.03	(2.83)	0.002	-56 -46 36
			1.000	3.01	(2.81)	0.002	-54 -68 16
			1.000	2.99	(2.79)	0.003	-62 -24 -8
			1.000	2.83	(2.66)	0.004	-62 -18 -24
			1.000	2.76	(2.60)	0.005	-32 -56 40

FIG. 4

## Increases in MCI



### Statistics: volume summary (p-values corrected for entire volume)

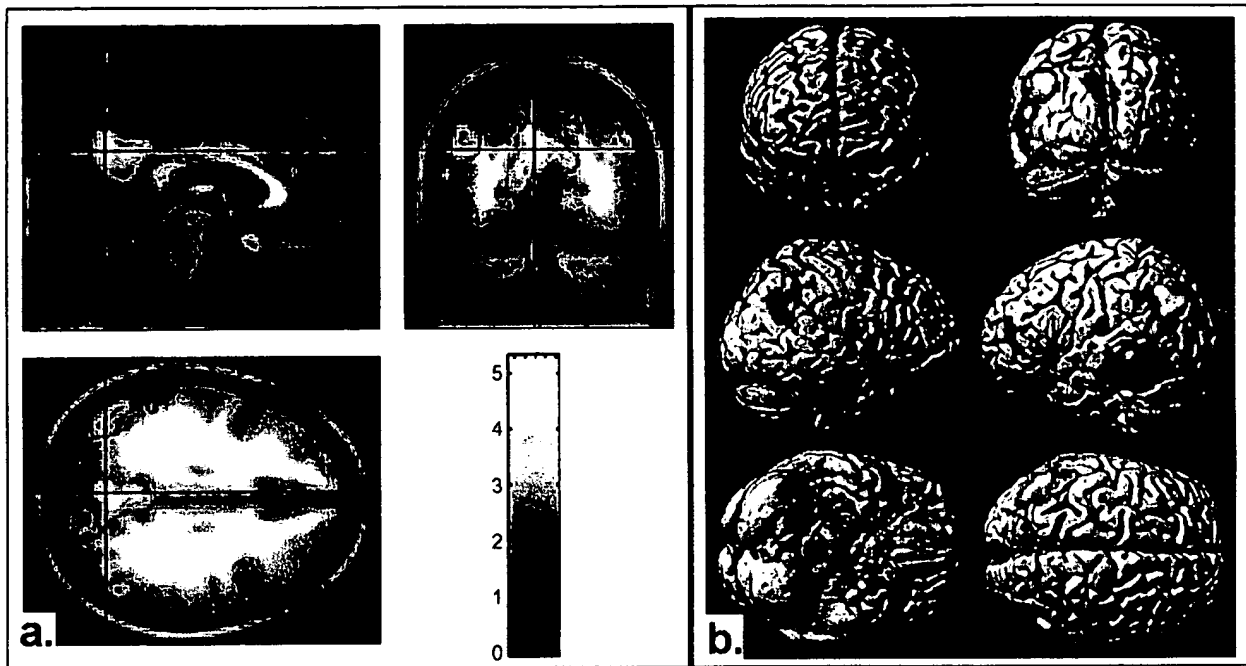
set-level		cluster-level			voxel-level				x,y,z (mm)		
p	c	p <sub>corrected</sub>	k <sub>E</sub>	p <sub>uncorrected</sub>	p <sub>corrected</sub>	T	(Z)	p <sub>uncorrected</sub>			
0.003	6	0.002	745	0.000	0.027	5.86	(4.82)	0.000	-16	-24	52
					0.528	4.48	(3.93)	0.000	-26	-26	66
					0.773	4.18	(3.71)	0.000	-6	-34	62
		0.318	188	0.026	0.120	5.23	(4.43)	0.000	26	-54	64
		0.003	678	0.000	0.202	5.00	(4.28)	0.000	10	-22	-30
					0.622	4.37	(3.85)	0.000	14	-38	-34
					0.925	3.92	(3.52)	0.000	-6	-28	-24
		0.001	873	0.000	0.379	4.68	(4.07)	0.000	34	-16	68
					0.434	4.60	(4.02)	0.000	26	-32	52
					0.596	4.40	(3.87)	0.000	14	-38	68
		0.530	138	0.051	0.837	4.08	(3.65)	0.000	62	12	36
					0.937	3.89	(3.50)	0.000	62	0	22
					0.994	3.59	(3.28)	0.001	62	0	34
		0.683	110	0.077	0.995	3.57	(3.26)	0.001	-6	-54	-16
					1.000	3.30	(3.05)	0.001	4	-50	-6

table shows at most local maxima > 8.0mm apart per cluster

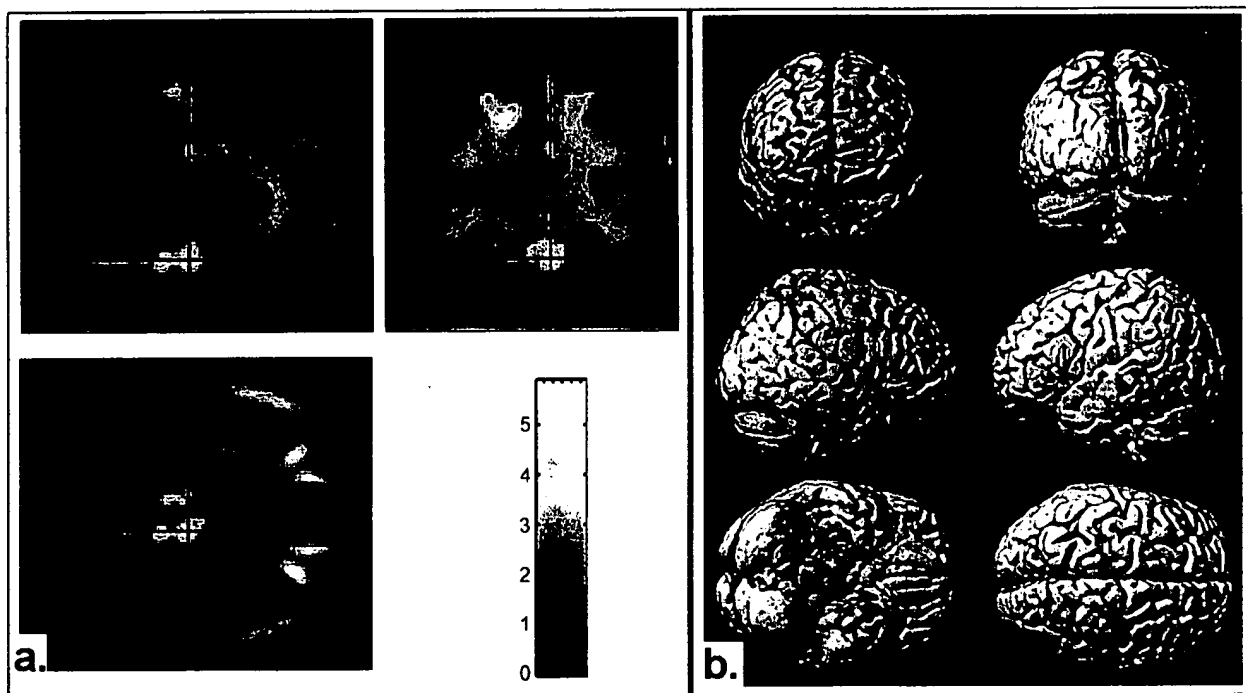
Height threshold:  $T = 3.00$ ,  $p = 0.003$  (1.000 corrected)  
 Extent threshold:  $k = 100$  voxels,  $p = 0.090$  (0.739 corrected)  
 Expected voxels per cluster,  $\langle k \rangle = 35.683$   
 Expected number of clusters,  $\langle c \rangle = 1.34$

Degrees of freedom = (1.0, 33.0)  
 Smoothness FWHM = 13.5 13.7 16.0 (mm) = 6.7 6.9 8.0 (voxels)  
 Search volume:  $S = 1815544 \text{ mm}^3 = 226943 \text{ voxels} = 559.8 \text{ resels}$   
 Voxel size: [2.0, 2.0, 2.0] mm (1 resel = 370.95 voxels)

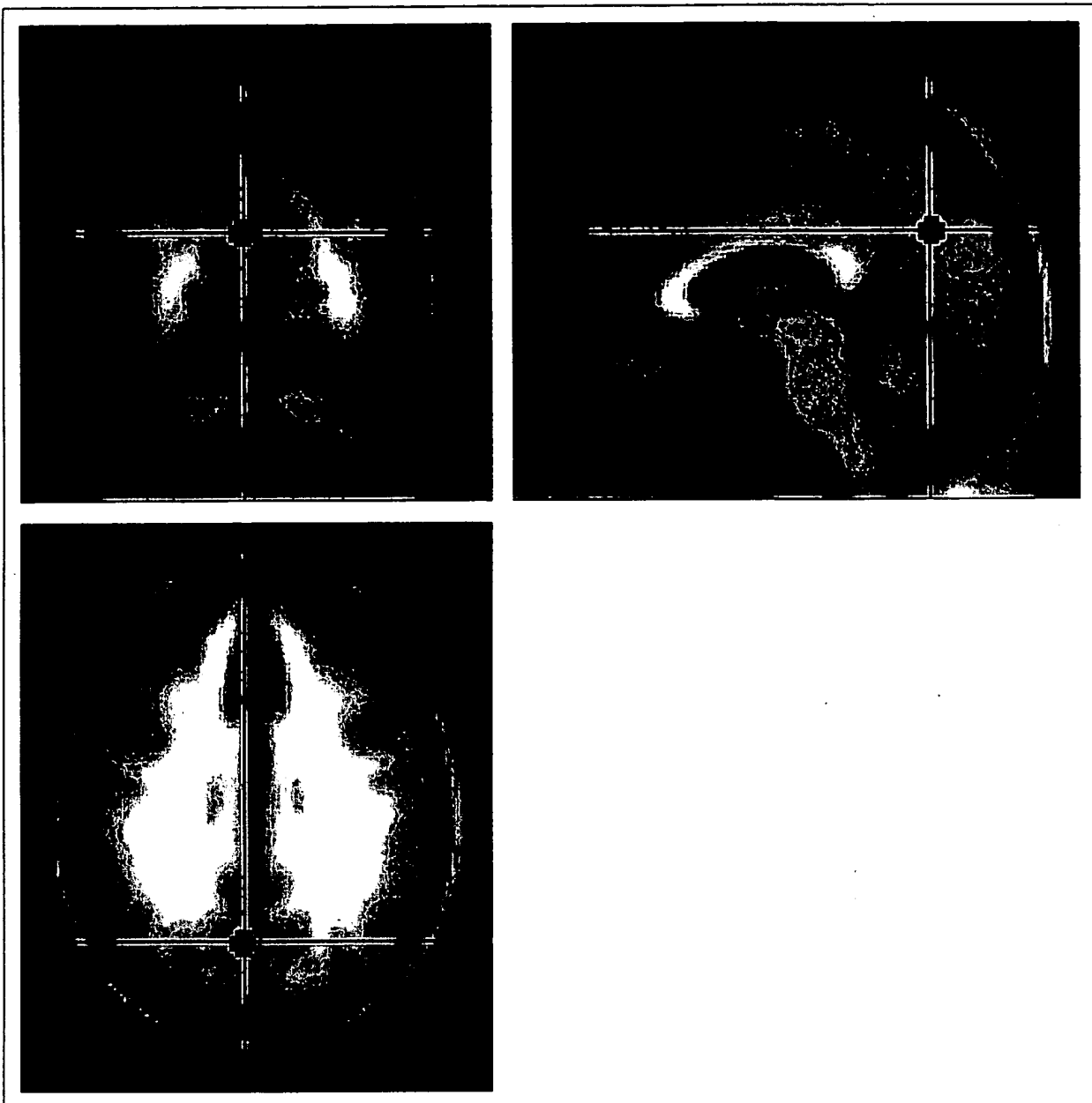
**Fig. 5**



**Fig. 6**



**Fig. 7**



**Fig. 8**

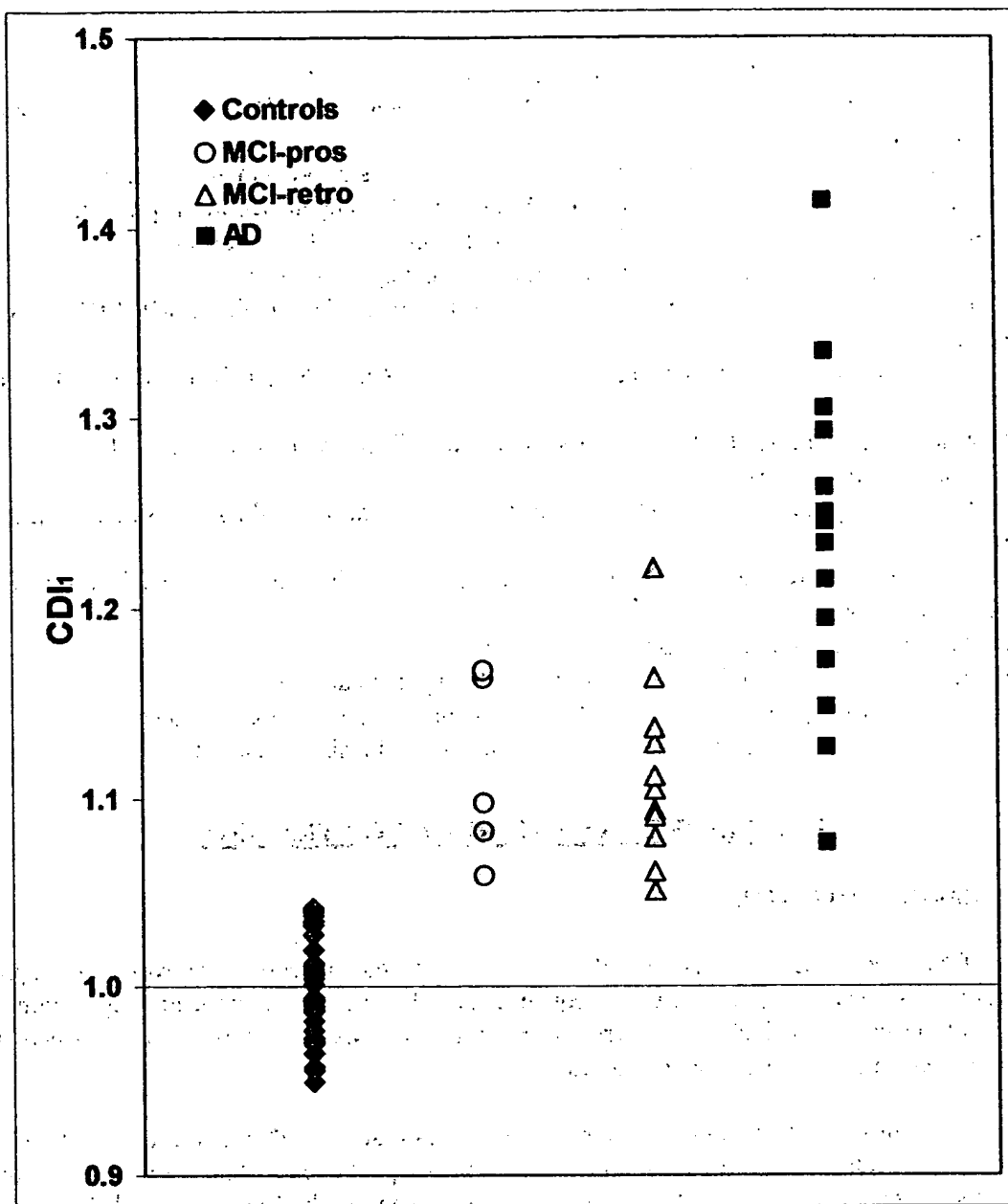


FIG. 9

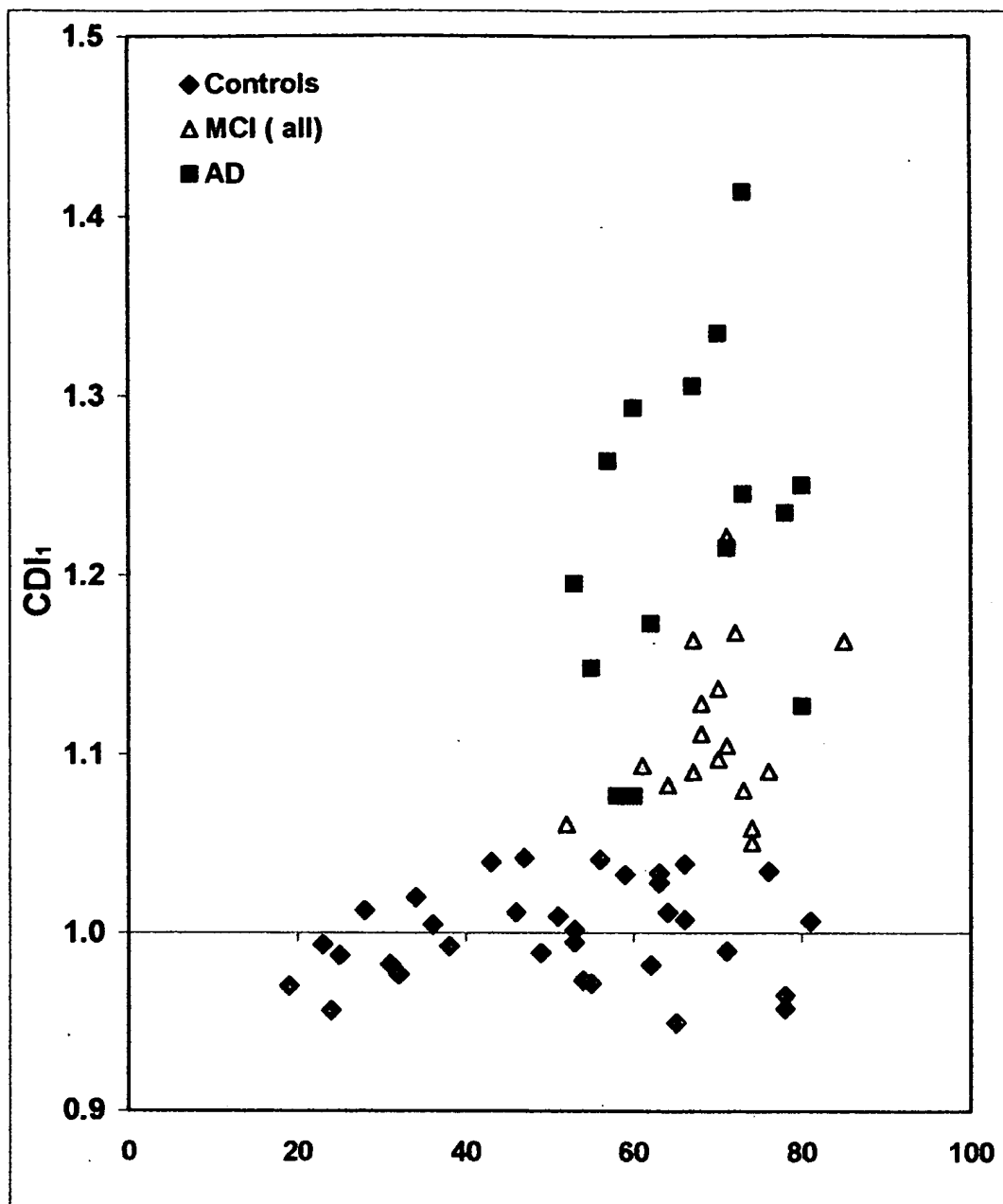


FIG. 10

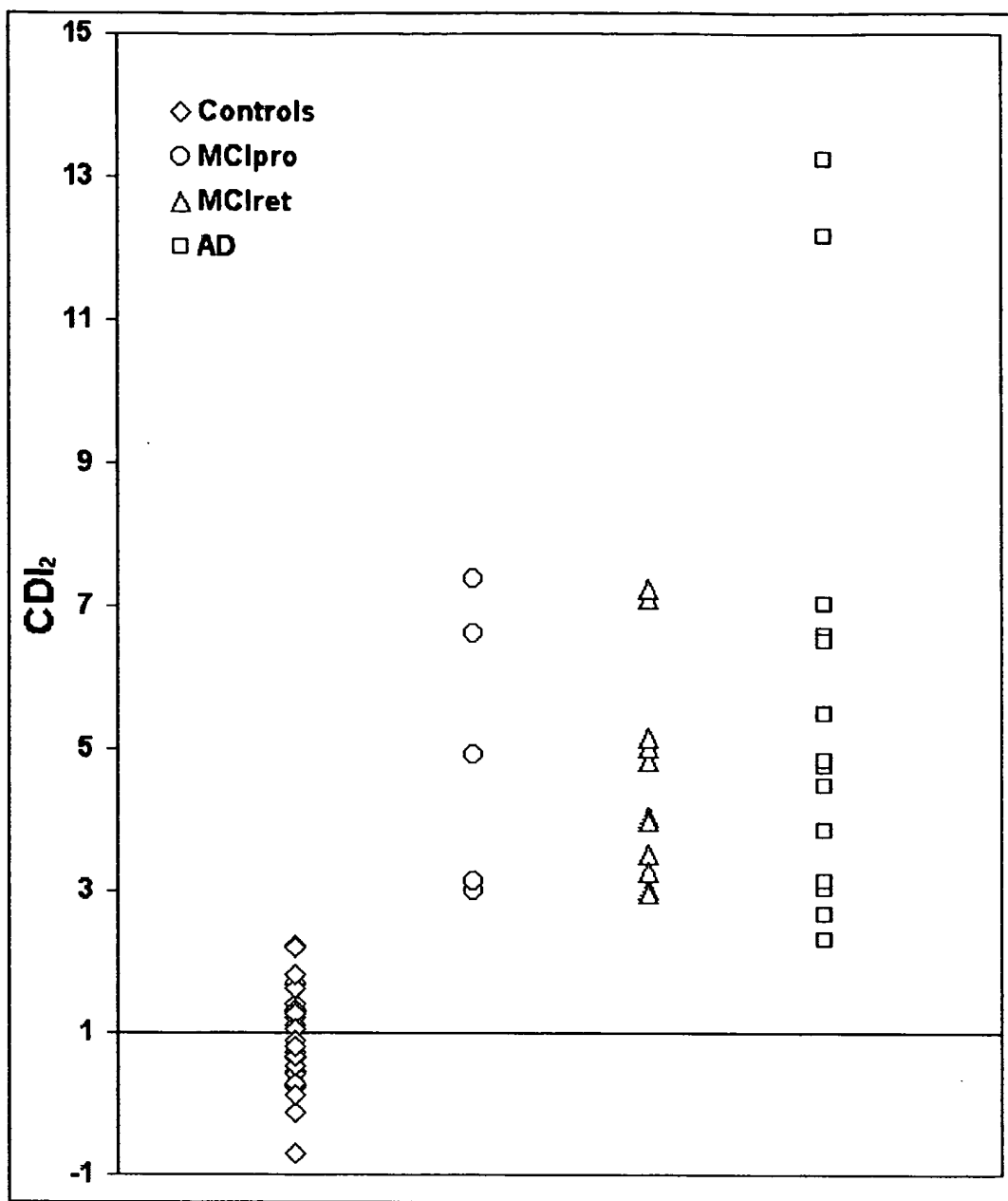


FIG. 11

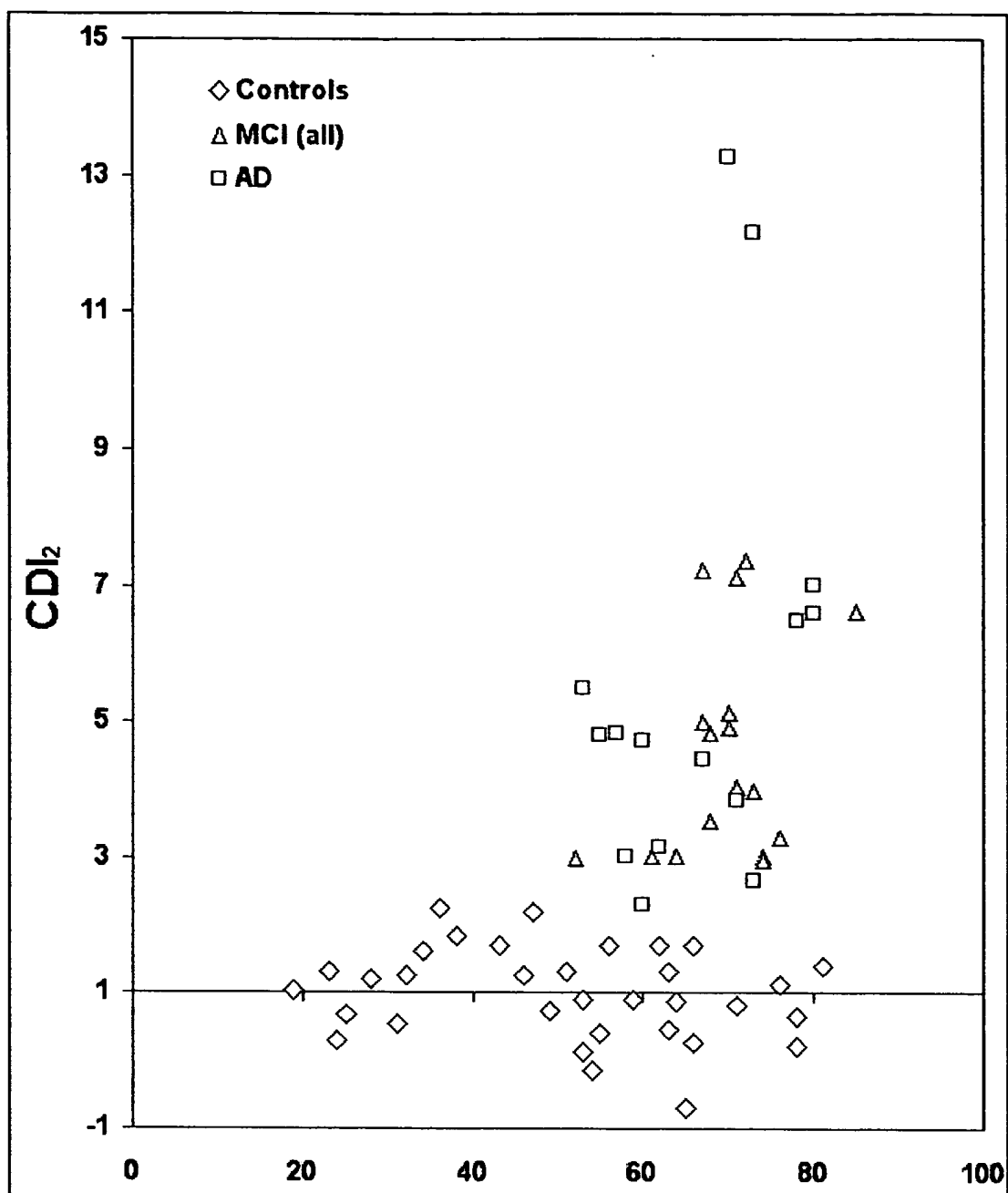


FIG. 12